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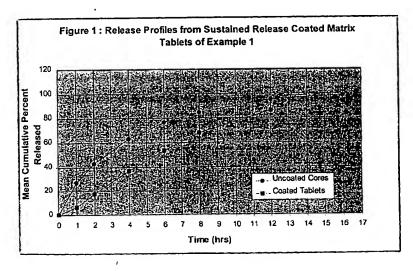
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(54) Title: DUAL MECHANISM TIMED RELEASE DOSAGE FORMS FOR LOW DOSE DRUGS



(57) Abstract: In accordance with the present invention, the release rate of a bioactive material from a hydrophilic polymer matrix core is modified by applying a water insoluble polymer membrane. The core composition as well as the membrane thickness are varied in order to achieve desired release profiles, from rapid release rate changing to near zero order release profiles with or without a lag time of up to 6 hours. The drug release from the dosage form of the invention is controlled by dual mechanism, viz., the dissolved drug first diffuses through the gelled polymer matrix and then through primarily a water insoluble polymer (semi-permeable) membrane, thereby providing the flexibility of modifying the release profiles including lag time for therapeutic agents for maximizing efficacy and patient compliance. As an illustration of this flexibility, the release profiles of Levalbuterol and Sotalol are described.



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

'INTERNATIONAL SEARCH REPORT

tional Application No PCT/US 01/10175

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K9/28 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, CHEM ABS Data, BIOSIS C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages EP 0 664 118 A (YOSHITOMI PHARMACEUTICAL) 1-11.18. X 19 26 July 1995 (1995-07-26) page 4, line 9 -page 6, line 2 page 8; example 2 US 4 871 549 A (UEDA YOSHIO ET AL) 1-11,18,χ 19 3 October 1989 (1989-10-03) column 1, line 50 -column 2, line 30 column 7 -column 8; examples 1-3 1-10,18,EP 0 793 959 A (TAKEDA CHEMICAL INDUSTRIES χ LTD) 10 September 1997 (1997-09-10) column 9 -column 10; example 1 column 4, line 3 - line 33 -/--Patent family members are listed in annex. Further documents are listed in the continuation of box C. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the *A* document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-*O* document reterring to an oral disclosure, use, exhibition or ents, such combination being obvious to a person skilled other means document published prior to the international filing date but later than the priority date claimed *A* document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 15/11/2001 7 November 2001 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040. Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

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